



US010125140B1

(12) **United States Patent**  
**Purro et al.**

(10) **Patent No.:** US 10,125,140 B1  
(45) **Date of Patent:** Nov. 13, 2018

(54) **CRYSTALLINE FORMS OF A BRUTON'S TYROSINE KINASE INHIBITOR**(71) Applicant: **Pharmacyclics LLC**, Sunnyvale, CA (US)(72) Inventors: **Norbert Purro**, Los Gatos, CA (US); **Mark S. Smyth**, Foster City, CA (US); **Erick Goldman**, Concord, CA (US); **David D. Wirth**, Oak Ridge, NC (US)(73) Assignee: **Pharmacyclics LLC**, Sunnyvale, CA (US)

(\* ) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: 16/036,258

(22) Filed: Jul. 16, 2018

**Related U.S. Application Data**

(60) Continuation of application No. 15/900,660, filed on Feb. 20, 2018, which is a continuation of application No. 15/887,744, filed on Feb. 2, 2018, which is a continuation of application No. 15/645,319, filed on Jul. 10, 2017, which is a continuation of application No. 15/497,896, filed on Apr. 26, 2017, now Pat. No. 9,725,455, which is a continuation of application No. 15/386,118, filed on Dec. 21, 2016, now Pat. No. 9,713,617, which is a division of application No. 14/405,317, filed as application No. PCT/US2013/043888 on Jun. 3, 2013, now Pat. No. 9,540,382.

(60) Provisional application No. 61/655,381, filed on Jun. 4, 2012.

(51) **Int. Cl.**

<i>A61K 31/519</i>	(2006.01)
<i>C07D 487/04</i>	(2006.01)
<i>A61K 9/20</i>	(2006.01)
<i>A61K 45/06</i>	(2006.01)
<i>B65D 75/36</i>	(2006.01)
<i>A61K 9/00</i>	(2006.01)
<i>A61K 9/48</i>	(2006.01)
<i>A61J 1/03</i>	(2006.01)

(52) **U.S. Cl.**

CPC .....	<i>C07D 487/04</i> (2013.01); <i>A61J 1/035</i> (2013.01); <i>A61K 9/0053</i> (2013.01); <i>A61K 9/2013</i> (2013.01); <i>A61K 9/2018</i> (2013.01); <i>A61K 9/2054</i> (2013.01); <i>A61K 9/4825</i> (2013.01); <i>A61K 9/4858</i> (2013.01); <i>A61K 9/4866</i> (2013.01); <i>A61K 31/519</i> (2013.01); <i>A61K 45/06</i> (2013.01); <i>B65D 75/36</i> (2013.01); <i>C07B 2200/13</i> (2013.01)
-----------	--

(58) **Field of Classification Search**

CPC .....	<i>A61K 31/519</i>
USPC .....	514/258.1

See application file for complete search history.

(56)

**References Cited**

## U.S. PATENT DOCUMENTS

4,824,982 A	4/1989	Vahlensieck et al.
5,033,252 A	7/1991	Carter
5,052,558 A	10/1991	Carter
5,145,684 A	9/1992	Liversidge et al.
5,323,907 A	6/1994	Kalvelage
5,397,787 A	3/1995	Buzzetti et al.
5,593,997 A	1/1997	Dow et al.
6,160,010 A	12/2000	Uckun et al.
6,221,900 B1	4/2001	Uckun et al.
6,303,652 B1	10/2001	Uckun et al.
6,306,897 B1	10/2001	Uckun et al.
6,326,469 B1	12/2001	Ullrich et al.
6,410,054 B1	6/2002	Thosar et al.
6,506,769 B2	1/2003	Snow et al.
6,660,744 B1	12/2003	Hirst et al.
6,753,348 B2	6/2004	Uckun et al.
6,770,639 B2	8/2004	Snow et al.
6,921,763 B2	7/2005	Hirst et al.
7,138,420 B2	11/2006	Bentzien et al.
7,332,497 B2	2/2008	Hirst et al.
7,514,444 B2	4/2009	Honigberg et al.
7,718,662 B1	5/2010	Chen et al.
7,732,454 B2	6/2010	Verner
7,741,330 B1	6/2010	Chen et al.
7,825,118 B2	11/2010	Honigberg et al.
7,960,396 B2	6/2011	Honigberg et al.
8,008,309 B2	8/2011	Honigberg et al.
8,088,781 B2	1/2012	Honigberg et al.
8,124,126 B2	2/2012	Bosse et al.
8,158,786 B2	4/2012	Honigberg et al.

(Continued)

## FOREIGN PATENT DOCUMENTS

CN	101610676 A	12/2009
CN	103121999 A	5/2013

(Continued)

## OTHER PUBLICATIONS

"Imbruvica," EPAR Summary for the Public, European Medicines Agency Science Medicines Health last updated Aug. 2016, retrieved from: <[http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/003791/human\\_med\\_001801.jsp&mid=WC0b01ac058001d124](http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/003791/human_med_001801.jsp&mid=WC0b01ac058001d124)>.

ACS 2015 (<http://www.cancer.org/cancer/non-hodgkinlymphoma/detailedguide/non-hodgkin-lymphoma-types-of-non-hodgkinlymphoma>).

(Continued)

*Primary Examiner* — Raymond J Henley, III(74) *Attorney, Agent, or Firm* — Foley Hoag LLP**ABSTRACT**

Described herein is the Bruton's tyrosine kinase (Btk) inhibitor 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-1-one, including crystalline forms, solvates and pharmaceutically acceptable salts thereof. Also disclosed are pharmaceutical compositions that include the Btk inhibitor, as well as methods of using the Btk inhibitor, alone or in combination with other therapeutic agents, for the treatment of autoimmune diseases or conditions, heteroimmune diseases or conditions, cancer, including lymphoma, and inflammatory diseases or conditions.